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EXAMINER

WOITACH, JOSEPH T

ART UNIT

PAPER NUMBER

1632

DATE MAILED: 12/04/2001

18

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/230,929

Applicant(s)

KLEINSCHMIDT ET AL.

Examiner

Joseph T. Voitach

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 17 September 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 14-66 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14-66 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

Art Unit: 1632

***Request for Continued Examination***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 17, 2001, paper number 17, has been entered.

**DETAILED ACTION**

Please note that the Examiner of record and art unit has changed. The Examiner of record is now **Joseph T. Voitach** and the group art unit is now **1632**.

This application is a 371 national stage filing of PCT/DE97/01629, filed July 30, 1997, which claims benefit to foreign application 196 31 357.0 filed August 2, 1996 in Germany.

Applicants' amendment filed July 24, 2001, paper number 14, has been entered. The abstract has been entered. The title has been amended. Claims 14, 49, 50, 52, 53, 61-63, 65 and 66 have been amended. Claims 14-66 are pending and currently under examination.

Art Unit: 1632

### *Specification*

Previously, the disclosure was objected to for several informalities which appeared to be a consequence of the translation. Applicants have supplied a substitute specification correcting and clarifying the issues raised in the objection. The substitute specification has been reviewed and found acceptable. Applicants' substitute specification filed July 24, 2001, paper 15, has been entered.

### *Claim Objections*

Claim 66 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn.

Applicant has amended the claim to place the claim in proper dependent form, further limiting the subject matter of claim 65 from which it depends which has obviated the basis of the objection. Therefore, the rejection is withdrawn.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 62-64 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vaccine composition comprising an AAV vector as set

Art Unit: 1632

forth in claim 14 and an auxiliary agent, does not reasonably provide enablement for vaccine wherein the vector is contained or presented in a cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants point out that the specification teaches the vector encompassed by claim 14. Further, Applicants point to specific passages in the disclosure for support of generating and delivering a vaccine wherein the vector expressing the antigen is present in a cell (specification page 5; lines 2-5). Further, Applicants state that tumor cell vaccines are well known to those skilled in the art. Accordingly, Applicants' argue that one of skill in the art would readily understand that the Applicants were at the time of filing in possession of a tumor cell vaccine encompassed by the claims. See Applicants' amendment, pages 8-9. Applicants' arguments have been fully considered but not found persuasive.

In the basis of the previous rejection, Examiner clearly pointed out the failure of the instant disclosure to provide the necessary guidance on how to make and use a cellular based vaccine. In particular, there is no clear guidance on determining a tumor or pre-tumor cell associated with HPV infection. Further, there is no specific guidance on how to 'inactivate' a cell, nor how the composition would be administered. Finally, given the unpredictability of any antigen to function as a vaccine, the disclosure fails to provide a nexus between suggesting the delivery of a cell based vaccine and establishing that said composition could function as a

Art Unit: 1632

vaccine. The teachings pointed to by Applicants in the instant disclosure for support of an enabling disclosure are only general statements suggesting that the composition can be used. The art recognized obstacles for cell based therapies underscores the need of teachings in the specification that would provide the artisan with specific treatment regimens that achieve a therapeutic benefit; however, the specification does not provide such guidance and fails to provide any correlation between specific amounts of the composition to be delivered, routes of delivery for the re-implantation or administration of the cells, or means of obtaining tumor or pre-tumor cells to practice the claimed invention. Without such guidance in the specification and the lack of correlative working examples, the claims would require an undue amount of experimentation without a predictable degree of success on the part of the skilled artisan.

The instant invention, as claimed, falls under the "germ of an idea" concept defined by the CAFC. The court has stated that "patent protection is granted in return for an enabling disclosure, not for vague intimations of general ideas that may or may be workable". The court continues to say that "tossing out the mere germ of an idea does not constitute an enabling disclosure" and that "the specification, not knowledge in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement". (See *Genentech inc v. Novo Nordisk A/S* 42 USPQ2d 1001, at 1005). The claimed methods of transfer constitute such a "germ of an idea".

Thus, in view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have

Art Unit: 1632

required undue experimentation to practice the invention as claimed, and therefore, the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-48, 51, 52 and 60-66 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

Applicants' amendments to the claims have obviated the basis of the rejection. Specifically, Applicants argue that it would not be undue experimentation to generate fusion proteins comprising a fragment of a HPV structural gene and a HPV early gene which would meet the limitation of 'non-transforming' as recited in the instant claims. Examiner agrees with Applicants arguments. Further, Examiner would point out that unlike E6 and E7, any of the full length ORF of E1-E5 would satisfy the limitation of non-transforming because they are known in the art not to have any transforming capabilities. In view of Applicants' amendments, the state of the art and Applicants' arguments, the rejection is withdrawn.

***Claim Rejections - 35 USC § 103***

Art Unit: 1632

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14-25, 27-30, 32, 34, 36, 38, 40, 42-60 65 and 66 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Donnelly *et al.* and Johnson.

Applicants agree that the teachings of argue that Donnelly *et al.* and Johnson provide the teachings and guidance for a fusion protein of element (a), however argue that there is no teaching for a fusion protein which is non-transforming for element (b). Applicants point out that full length E7-ORF could be transforming when expressed in an AAV vector and the instant disclosure provides the guidance wherein only a non-transforming portion of E7-ORF is expressed. See Applicants' amendment, pages 11-12. Applicants' arguments have been fully considered, but not found persuasive.

Examiner agrees that expression of the full length E7-ORF could cause transformation of certain cell types under certain condition, however E1-E5 are also specifically taught. As noted



Art Unit: 1632

above, E1-E5 are known in the art not to be involved in transformation. Further, Examiner would note that the art teaches that E6 and E7 have transforming capabilities only under certain circumstances and in certain cell types, and as such even the full length E6 and E7 ORFs could satisfy the limitation of non-transforming given the correct context of use. Notwithstanding E6 and E7, the instant claims recite and encompass E1-E5 which are specifically taught in the cited references. Since E1-E5 meet the limitation of non-transforming, the instant claims are anticipated by the teachings of Donnelly *et al.* and Johnson, and the rejection is maintained.

Claims 14-60 65 and 66 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Donnelly *et al.*, Johnson as applied to claims 14-25, 27-30, 32, 34, 36, 38, 40, 42-60 65 and 66, in further view of Whittle *et al.*

Applicants agree that the teachings of argue that Donnelly *et al.*, Johnson and Whittle *et al.* provide the teachings and guidance for a fusion protein of element (a), however argue that there is no teaching for a fusion protein which is non-transforming for element (b). Applicants point out that full length E7-ORF could be transforming when expressed in an AAV vector and the instant disclosure provides the guidance wherein only a non-transforming portion of E7-ORF is expressed. See Applicants' amendment, page 12. Applicants' arguments have been fully considered, but not found persuasive.

As noted above, Examiner agrees that expression of the full length E7-ORF could cause transformation of certain cell types under certain condition, however E1-E5 are known in the art

Art Unit: 1632

not to be involved in transformation. Notwithstanding the inability of E6 and E7 to transform any cell type encompassed by the claim, the instant claims recite and encompass E1-E5 which are specifically taught in the cited references. Since E1-E5 meet the limitation of non-transforming, the instant claims are anticipated by the teachings of Donnelly *et al.*, Johnson, and Whittle *et al.*, and the rejection is maintained.

Claims 16, 18, 20 and 50 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Donnelly *et al.* and Johnson as applied to claims 14-25, 27-30, 32, 34, 36, 38, 40, 42-60 65 and 66, in further view of Gissmann *et al.*

Applicants point out that full length E7-ORF could be transforming when expressed in an AAV vector and the instant disclosure provides the guidance wherein only a non-transforming portion of E7-ORF is expressed. See Applicants' amendment, pages 12-13, bridging paragraphs. Applicants' arguments have been fully considered, but not found persuasive.

As noted above, Examiner agrees that expression of the full length E7-ORF could cause transformation of certain cell types under certain condition, however E1-E5 are known in the art not to be involved in transformation. Notwithstanding the inability of E6 and E7 to transform any cell type encompassed by the claim, the instant claims recite and encompass E1-E5 which are specifically taught in the cited references. Gissmann *et al.* was introduced to demonstrate that at the time of filing various types of HPV, specifically HPV33, HPV35 and HPV45, were known and used in the art for the generation of HPV fusion proteins. Since E1-E5 meet the limitation of

Art Unit: 1632

non-transforming, the instant claims are anticipated by the teachings of Donnelly *et al.*, Johnson, and Gissmann *et al.*, and the rejection is maintained.

Claim 61 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Donnelly *et al.* and Johnson as applied to claims 14-25, 27-30, 32, 34, 36, 38, 40, 42-60 65 and 66, in further view of Stanley *et al.*

Applicants point out that full length E7-ORF could be transforming when expressed in an AAV vector and the instant disclosure provides the guidance wherein only a non-transforming portion of E7-ORF is expressed. See Applicants' amendment, pages 12-13, bridging paragraphs. Applicants' arguments have been fully considered, but not found persuasive.

As noted above, Examiner agrees that expression of the full length E7-ORF could cause transformation of certain cell types under certain condition, however E1-E5 are known in the art not to be involved in transformation. Notwithstanding the inability of E6 and E7 to transform any cell type encompassed by the claim, the instant claims recite and encompass E1-E5 which are specifically taught in the cited references. Stanley *et al.* was introduced to demonstrate that at the time of filing various adjuvants were used in compositions comprising HPV proteins in attempt to induce an immune response. Since E1-E5 meet the limitation of non-transforming, the instant claims are anticipated by the teachings of Donnelly *et al.*, Johnson, and Gissmann *et al.*, and the rejection is maintained.

Art Unit: 1632

*Conclusion*

No claim allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

Art Unit: 1632

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen M. Hauda, can be reached at (703)305-6608.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Kay Pinkney whose telephone number is (703)306-3553.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

*Deborah Crouch*

Joseph T. Voitach

DEBORAH CROUCH  
PRIMARY EXAMINER  
GROUP 1800/1630